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Collateral Ventilation: Friend or Foe in Patients with Severe Emphysema

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Over the past decade, significant improvements have been made in developing nonpharmacological interventions to enhance lung mechanics in patients with severe emphysema [1]. Collateral ventilation has been an influential factor for some of the therapies and is defined as ventilation of the alveoli via pathways that bypass the normal bronchial airways. The initial randomized controlled trials with endobronchial valves failed to demonstrate clinically meaningful results as a proportion of the treated patients had collateral ventilation and hence did not develop lobar atelectasis [2]. Once the role of collateral ventilation was appreciated and patients were more carefully selected on the basis of formal measurements, remarkable benefits have been observed with mean improvements in FEV_1 between 20 and 25% [3–5]. Such is the importance of collateral ventilation that surrogate markers for collateral ventilation such as fissure integrity are formally assessed on the computed tomography scans at the screening stage and in the majority of patients formal measurements of collateral ventilation are performed by the Chartis procedure as recommended by the latest Best Practice Guidelines [6].

A significant proportion of patients with emphysema have collateral ventilation and hence alternative bronchoscopic techniques have been developed that work independently of this physiological phenomenon. For this patient group, both endobronchial coils [7, 8] as well as sclerosing therapies [9–11] have shown potential as treatment options. Collateral ventilation thus seems the most important denominator in both chronic obstructive pulmonary disease and in bronchoscopic lung volume reduction. Where there is a dominant chronic obstructive pulmonary disease component, there is mucosal inflammation, bronchospasm, irregular airways, and mucus plugging. In this situation, the resistance of the airways is usually high leading to progressive air trapping, hypoxemia and hypercapnia. With progressive emphysema, there is destruction of the alveolar parenchyma increasing both intra- and interlobar collateral ventilation. Very early studies in excised emphysematous lungs confirmed that the resistance to collateral flow is much lower than the resistance in the airways [12]. This allows the exchange of gas even in obstructed segments and may account for the relative preservation of hypoxemia in emphysema patients.

In the past, several attempts have been made to take advantage of the abundant presence of collateral ventilation in severe emphysema by creating fenestrations – a so-called "airway bypass" – between the areas of trapped air and places where this air can easily be released. Early

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work in this field both showed potential using a transthoracic airway bypass approach [13, 14], as well as creating a bronchoscopic transbronchial airway bypass [15].

To prove the safety and efficacy of creating extra-anatomic airway bypasses between the most diseased areas of the lung and the large airways which were supported by paclitaxel drug-eluting stents to ensure patency, a randomized, full sham-controlled, multicenter trial (the EASE trial) was performed in patients with severe homogeneous emphysema [16]. The EASE trial showed that the airway bypass improved patient outcomes directly after the procedure; however, the durability of the effects was limited, and outcomes for both the sham-controlled and treatment groups were similar long after the procedure. Although the concept of creating an airway bypass was proven in this trial, the loss of airway bypass patency due to several factors caused the loss of the observed initial benefit [16].

In this issue of *Respiration*, Snell et al. [17] report on a unique treatment in a unique patient population whom they were able to follow for years after treatment with a transthoracic airway bypass. Creating a transthoracic airway bypass comes with a number of potential issues, such as thoracic surgery to create the bypass, with initially significant subcutaneous emphysema, frequent change of the bypass tubing, frequent interventions to clear out the bypass channel and of course also local esthetical issues. However, this paper again shows the great potential of creating functional collateral channels allowing emphysematous lungs to more easily empty and by those means improve their dyspnea symptoms. Based on this long-term follow-up, earlier reports, and our own observations [16, 18], we can only encourage further innovation and development of – preferably endoscopic – techniques that will allow this therapeutic approach to become more widely applicable for our highly symptomatic severe emphysema patients. Especially homogeneous emphysema patients with a high level of tissue destruction and who do have interlobar collateral ventilation seem to be the target patients for this therapy.

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